WARNING: SERIOUS SKIN RASHES
Cases of life-threatening serious rashes, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and/or rash-related death, have been caused by Lamotrigine. The rate of serious rash is greater in pediatric patients than in adults. Additional factors that may increase the risk of rash include:

- coadministration with valproate
- exceeding recommended initial dose of Lamotrigine
- exceeding recommended dose escalation of Lamotrigine

Benign rashes are also caused by Lamotrigine; however, it is not possible to predict which rashes will prove to be serious or life threatening. Lamotrigine should be discontinued at the first sign of rash, unless the rash is clearly not drug related. Discontinuation of treatment may not prevent a rash from becoming life threatening or permanently disabling or disfiguring.

Please refer to the full Prescribing Information for Lamotrigine Tablets, USP for the complete boxed warning.

IMPORTANT SAFETY INFORMATION

Lamotrigine Tablets, USP are indicated for:

**Epilepsy**—adjunctive therapy in patients aged 2 years and older:
- partial-onset seizures
- primary generalized tonic-clonic seizures
- generalized seizures of Lennox-Gastaut syndrome

**Epilepsy**—monotherapy in patients aged 16 years and older: Conversion to monotherapy in patients with partial-onset seizures who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as the single AED.

**Bipolar disorder**: Maintenance treatment of bipolar I disorder to delay the time to occurrence of mood episodes in patients treated for acute mood episodes with standard therapy.

**LIMITATION OF USE**
Treatment of acute manic or mixed episodes is not recommended. Effectiveness of Lamotrigine in the acute treatment of mood episodes has not been established.

**CONTRAINDICATIONS**
Lamotrigine is contraindicated in patients who have demonstrated hypersensitivity to the drug or its ingredients.

**WARNINGS & PRECAUTIONS**

- **Cases of life-threatening serious rashes, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and/or rash-related death, have been caused by Lamotrigine.**
- The rate of serious rash is greater in pediatric patients than in adults. Refer to Lamotrigine - BOXED WARNING.
- Lamotrigine should not be abruptly discontinued. In patients with epilepsy there is a possibility of increasing seizure frequency. Unless safety concerns require a more rapid withdrawal, the dose of Lamotrigine should be tapered over a period of at least 2 weeks. Refer to Lamotrigine - DOSAGE AND ADMINISTRATION.

- **Hemophagocytic lymphohistiocytosis (HLH)** has occurred in adult and pediatric patients taking Lamotrigine. HLH is a life-threatening syndrome of pathologic immune activation characterized by clinical signs and symptoms of extreme systemic fibrosis. It is associated with high mortality rates if not recognized early and treated. HLH has presented with systemic inflammation (fever, rash, hepatoplenomegaly, and organ system dysfunction) and blood dyscrasias. Symptoms have been reported to occur within 8 to 24 days following the initiation of treatment. Patients who develop early manifestations of pathologic immune activation should be evaluated immediately, and a diagnosis of HLH should be considered.

- **Multitorgan hypersensitivity reactions**, also known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), have occurred with Lamotrigine. Some have been fatal or life threatening. DRESS typically, although not exclusively, presents with fever, rash, and/or lymphadenopathy in association with other organ system involvement, such as hepatitis, rashes, hematologic abnormalities, myositis, or myocarditis, sometimes resembling an acute viral infection. Eosinophilia is often present. This disorder is variable in its expression, and other organ systems not noted here may be involved. Fatalities associated with acute multorgan failure and various degrees of hepatic failure have been reported. Prior to initiation of treatment with Lamotrigine, the patient should be instructed that a rash or other signs or symptoms of hypersensitivity should be reported. Merit may herald a serious medical event and that the patient should report any such occurrence to a healthcare provider immediately.

- **There have been reports of blood dyscrasias that may or may not be associated with multorgan hypersensitivity** (also known as DRESS). These have included neutropenia, leukopenia, anemia, thrombocytopenia, pancytopenia, and, rarely, aplastic anemia and pure red cell aplasia.

- **Antiepileptic drugs (AEDs)**, including Lamotrigine, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Anyone prescribing Lamotrigine must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Patients, their caregivers, and families should be informed of the potential for serious outcomes of untreated epilepsy and atherThan causes, patients should also be evaluated for other causes of meningitis and treated as appropriate.

- **Medication errors involving Lamotrigine have occurred.** In particular, the name Lamotrigine or lamotrigine can be confused with the names of other commonly used medications. Medication errors may also occur between the different formulations of Lamotrigine.

- **Some estrogen-containing oral contraceptives have been shown to decrease serum concentrations of lamotrigine.** Dosage adjustments will be necessary in most patients who start or stop estrogen-containing oral contraceptives while taking Lamotrigine.

- **Valid estimates of the incidence of treatment-emergent status epilepticus among patients treated with Lamotrigine are difficult to obtain because reports participating in clinical trials did not employ identical rules for identifying cases. At a minimum, 7 of 2,343 adult patients had episodes that could unequivocally be described as status epilepticus. In addition, a number of reports of variably defined episodes of severe exacerbation (e.g., seizure clusters, seizure flurries) were made.**

- **During the premarketing development of Lamotrigine, 20 sudden and unexplained deaths were recorded among a cohort of 4,700 patients with epilepsy (5,747 patient-years of exposure).** The rate of serious rash is greater in pediatric patients than in adults. Refer to Lamotrigine - BOXED WARNING.

- **Because valproate reduces the clearance of lamotrigine, the dosage of Lamotrigine in the presence of valproate is less than half of that required in its absence.**

- **Because lamotrigine is eliminated in breast milk, it could accumulate in the milk of nursing mothers. This could result in toxicity in the nursing infant.**

- **There have been reports of decreased lamotrigine concentrations during hospitalization and/or post partum.**

- **Because lamotrigine is metabolized predominantly by glucuronidation conjugation, drugs that are known to induce or inhibit glucuronidation may affect the apparent clearance of lamotrigine and doses of Lamotrigine may require adjustment based on clinical response.**

**DOZING GUIDELINES & CONSIDERATIONS**

- Refer to the Lamotrigine - DOSAGE AND ADMINISTRATION section of the full prescribing information for recommended dosing guidelines for Lamotrigine.

- There are a number of significant drug interactions with Lamotrigine. Refer to the Lamotrigine - DRUG INTERACTIONS section of the full prescribing information.

**ADVERSE REACTIONS**

- See the ADVERSE REACTIONS section of the Lamotrigine full prescribing information for adverse reaction rates from clinical trials conducted under widely varying conditions.

- **The most common adverse reactions** (incidence ≥5%) in adult epilepsy clinical studies were diziness, ataxia, somnolence, headache, diplopia, blurred vision, nausea, vomiting, and rash. The most common adverse reactions (incidence ≥5%) in pediatric clinical studies included vomiting, infection, rash, fever, somnolence, accidental injury, diziness, abdominal pain, diarrhea, nausea, ataxia, asthenia, bronchitis, flu syndrome, diplopia, and tremor.

- **The most common adverse reactions** (incidence ≥5%) in adult bipolar clinical studies were nausea, insomnia, somnolence, back pain, fatigue, rash, rhinitis, abdominal pain, and xerostomia.

To report SUSPECTED ADVERSE REACTIONS, contact OWP Pharmaceuticals Inc. at 1-800-273-6729 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please refer to the full Prescribing Information for Lamotrigine Tablets, including Medication Guide at www.owppharma.com/starter-kit.

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